was left intact. After the synthesis, the contents of the synthesis cartridge (1 μmole) were transferred to a Pyrex vial and the oligonucleotide was cleaved from the controlled pore glass (CPG) using 5 mL of 30% ammonium hydroxide (NH_4OH) for approximately 16 hours at 55 °C.

c. Oligonucleotide Purification

[0209] After the deprotection step, the samples were filtered from CPG using Gelman 0.45 μm nylon acrodisc syringe filters. Excess NH_4OH was evaporated away in a Savant AS160 automatic SpeedVac. The crude yield was measured on a Hewlett Packard 8452A Diode Array Spectrophotometer at 260 nm. Crude samples were then analyzed by mass spectrometry (MS) on a Hewlett Packard electrospray mass spectrometer. Trityl-on oligonucleotides were purified by reverse phase preparative high performance liquid chromatography (HPLC). HPLC conditions were as follows: Waters 600E with 991 detector; Waters Delta Pak C4 column (7.8X300mm); Solvent A: 50 mM triethylammonium acetate (TEA-Ac), pH 7.0; B: 100% acetonitrile; 2.5 mL/min flow rate; Gradient: 5% B for first five minutes with linear increase in B to 60% during the next 55 minutes. Fractions containing the desired product (retention time = 41 min. for DMT-ON-16314; retention time = 42.5 min. for DMT-ON-16315) were collected and the solvent was dried off in the SpeedVac. Oligonucleotides were detritylated in 80% acetic acid for approximately 60 minutes and lyophilized again. Free trityl and excess salt were removed by passing detritylated oligonucleotides through Sephadex G-25 (size exclusion chromatography) and collecting appropriate samples through a Pharmacia fraction collector. The solvent was again evaporated away in a SpeedVac. Purified oligonucleotides were then analyzed for purity by CGE, HPLC (flow rate: 1.5 mL/min; Waters Delta Pak C4 column, 3.9X300mm), and MS. The final yield was determined by spectrophotometer at 260 nm.

[0210] The synthesized oligonucleotides and their physical characteristics are shown, respectively, in Tables VIII and IX. All nucleosides with an asterisk contain MMI linkage.

Table VIII
ICAM-1 Oligonucleotides Containing MMI Dimers Synthesized for *in Vivo* Nuclease and Pharmacology Studies.

SEQ ID NO. #	(ISIS)#	Sequence (5'-3')	Backbone	2'-Chemistry
21	(16134)	TGC ATC CCC CAG GCC ACC	P=S, MMI	Bis-2'-OMe-MMI, A*T 2'-H
22	(16315)	T*GC ATC CCC CAG GCC	P=S, MMI	Bis-2'-OMe-MMI, ACCA*T2'-H
23	(3082)	TGC ATC CCC CAG GCG ACC	P=S	2'-H, single AT mismatch
23	(13001)	TGC ATC CCC CAG GCC ACC	P=S	2'-H AT

Table IX
Physical Characteristics of MMI Oligomers Synthesized for Pharmacology, and *In Vivo* Nuclease Studies

SEQ ID NO. #	(ISIS)#	Sequence (5'-3')	Expected Mass (g)	Observed Mass (g)	HPLC Time (min)	Retn.
21	(16314)	TGC ATC CCC CAG GCC ACC A*T	6295	6297	23.9	
22	(16315)	T*G C ATC CCC CAG GCC ACC A*T	6302	6303	24.75	

[0211] HPLC Conditions: Waters 600E with detector 991; Waters C4 column (3.9X300mm); Solvent A: 50 mM TEA-Ac, pH 7.0; B: 100% acetonitrile; 1.5 mL/min. flow rate; Gradient: 5% B for first five minutes with linear increase in B to 60% during the next 55 minutes.

EXAMPLE 59

Synthesis of Sp Terminal Oligonucleotide

a. 3'-*O*-t-Butyldiphenylsilyl-thymidine (1)

[0212] 5'-*O*-Dimethoxytritylthymidine is silylated with 1 equivalent of t-butyldiphenylsilyl chloride (TBDPSCl) and 2 equivalents of imidazole in DMF solvent at room temperature. The 5'-protecting group is removed by treating with 3% dichloracetic acid in CH_2Cl_2.

b. 5'-*O*-Dimethoxytrityl-thymidin-3'-*O*-yl-N,N-diisopropylamino (S-pivaloyl-2-mercaptoethoxy) phosphoramidite (2)

[0213] 5'-*O*-Dimethoxytrityl thymidine is treated with bis-(N,N-diisopropylamino)-S-pivaloyl-2-mercaptoethoxy phosphoramidite and tetrazole in CH_2Cl_2/CH_3CN as described by Guzaev *et al., Bioorganic & Medicinal Chemistry Letters* **1998**, *8*, 1123) to yield the title compound.

c. 5'-*O*-Dimethoxytrityl-2'-deoxy-adenosin-3'-*O*-yl-N,N-diisopropylamino (S-pivaloyl-2-mercapto ethoxy) phosphoramidite (3)

[0214] 5'-*O*-Dimethoxytrityl-N-6-benzoyl-2'-deoxy-adenosine is phosphitylated as in the previous example to yield the desired amidite.

d. 3'-*O*-t-Butyldiphenylsilyl-2'-deoxy-N_2-isobutyryl-guanosine (4)

[0215] 5'-*O*-Dimethoxytrityl-2'-deoxy-N_2-isobutyryl-guanisine is silylated with TBDPSCl and imidazole in DMF. The 5'-DMT is then removed with 3% DCA in CH_2Cl_2.

e. $T_{(Sp)}G$ dimers and $T_{(S)}$ Phosphoramidite

[0216] Compounds **4** and **2** are condensed (1:1 equivalents) using 1H-tetrazole in CH_3CN solvent followed by sulfurization employing Beaucage reagent (*see, e.g.,* Iyer, *et al., J. Org. Chem.* **1990**, *55*, 4693). The dimers (TG) are separated by column chromatography and the silyl group is deprotected using t-butyl ammonium fluoride/THF to give Rp and Sp dimers of T_sG. Small amounts of these dimers are completely deprotected and treated with either P1 nuclease or snake venom phosphodiesterase. The R isomer is resistant to P1 nuclease and hydrolyzed by SVPD. The S isomer is resistant to SVPD and hydrolyzed P1 nuclease. The Sp isomer of the fully protected T_sG dimer is phosphitylated to give DMT-T-Sp-G-phosphoramidite.

f. A_sT Dimers and Solid Support Containing $A_{SP}T$ Dimer

[0217] Compounds **3** and **1** are condensed using 1H-tetrazole in CH_3CN solvent followed by sulfurization to give AT dimers. The dimers are separated by column chromatography and the silyl group is deprotected with TBAF/THF. The configurational assignments are done generally as in the previous example. The Sp isomer is then attached to controlled pore glass